

FIGURE 1A

Amino acid sequence of human CCR5 [SEQ ID NO: 1]:

1 MDYQVSSPIY DINYYTSEPC QKINVKQIAA RLLPPLYSLV FIFGFVGNML VILILINCKR
N-Terminus Transmembrane Domain 1

61 LKSMTDIYLL NLAISDLFFL LTVPFWAHYA AAQWDFGNIM CQLLTGLYFI GFFSGIFFII
LOOP 1 Transmembrane Domain 2 Loop 2 Transmembrane Domain 3

121 LLTIDRYLAV VHAVFALKAR TVTFGVVTSV ITWVVAVFAS LPGIIFTRSQ KEGLHYTCSS
Loop 3 Transmembrane Domain 4 Loop 4

181 HFPYSQYQFW KNFQTLKIVI LGLVLP LLVM VICYSGILKT LLRCRNEKKR HRAVRLIFTI
Transmembrane Domain 5 Loop 5

241 MIVYFLFWAP YNIVLLNLT QEFFGLNNCS SSNRLDQAMQ VTETLGMTHC CINPIIYAFV
Transmembrane Domain 6 Loop 6 Transmembrane Domain 7

301 GEKFRNYLLV FFOKHIARF CKCCSIFQQE APERASSVYT RSTGEQEISV GL
C-Terminus

FIGURE 1B

Peptide fragments derived from human CCR5 that are used as target peptides:

N-terminal fragment [SEQ ID NO: 8]:

MDYQVSSPIYDINYYTSEPCQKINVKQIAARLLPPL

Loop 4 fragment [SEQ ID NO: 9]:

TRSQKEGLHYTCSSHFPYSQYQFWKNFQTLKI

Loop 6 fragment [SEQ ID NO: 3]:

EFFGLNNCSSNRLDQAMQVTETLGMTHC

FIGURE 2A

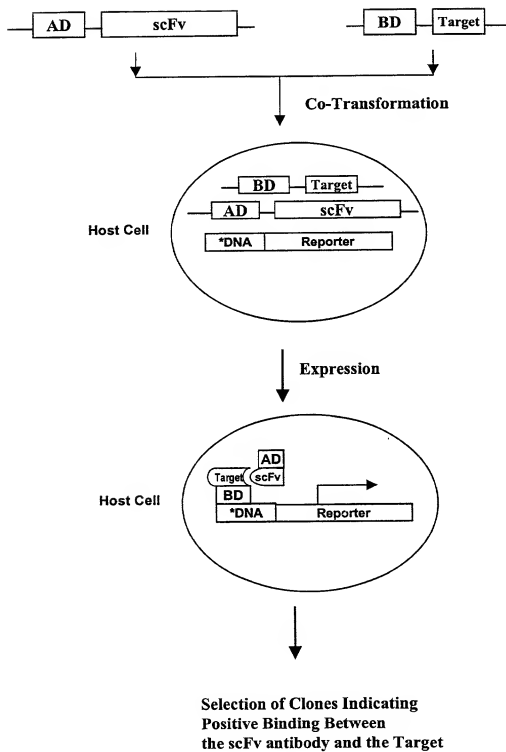


FIGURE 2B

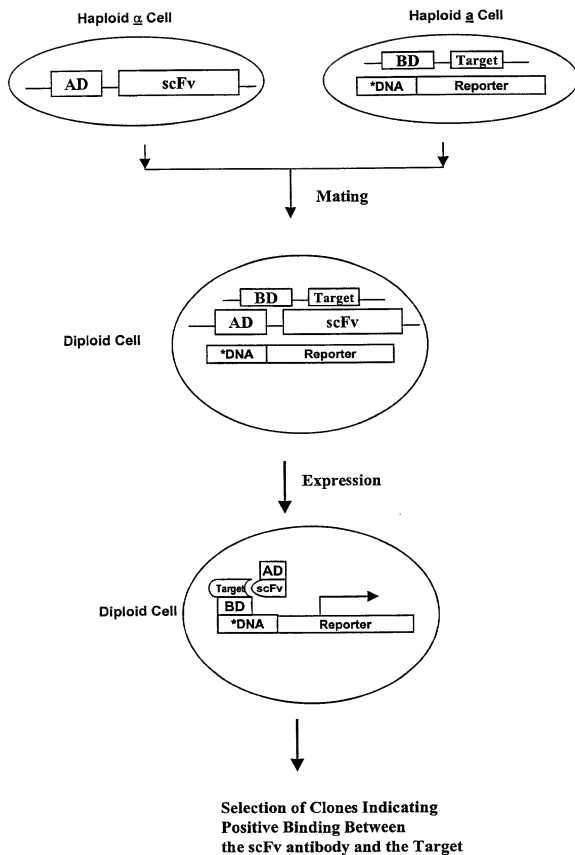


FIGURE 3

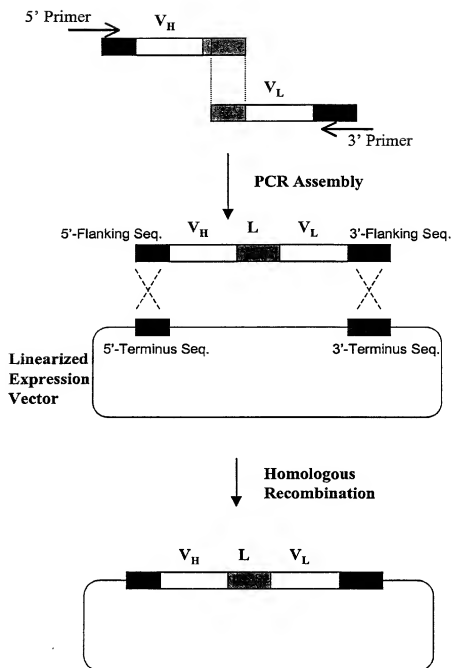


FIGURE 4

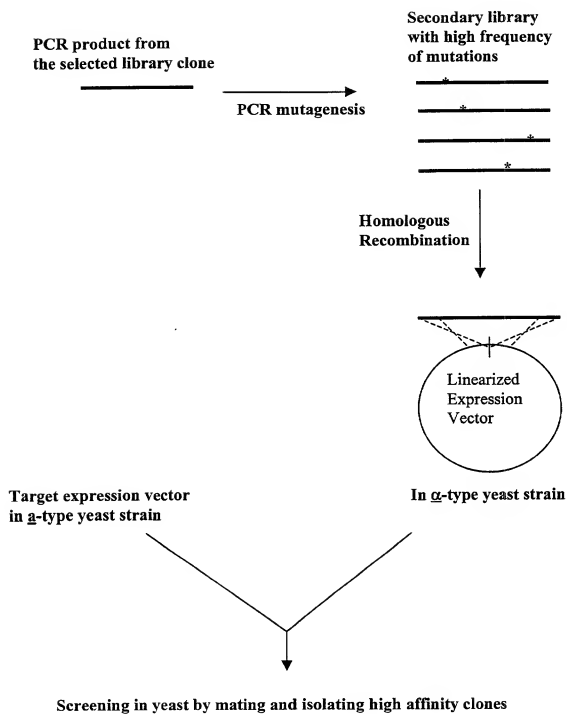


FIGURE 5 (cont.)

DNA sequence of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 20]:

CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGTCTTGGGGAACCCGTGTCCTCACCTGCGCTGTCTCTGGTGC
GTGCTTTAGTGGTATTATTGGAGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAGATCAATCATC
GTGGAAGCACTACTACAAACCGTCCCTCGACGGTCGAGTCACCATATCATTAGACACATCTACCAACAGATCTCCCTT
AAACTGACCTCTATGACCCGCCGCGACACGGCCGTGTATTACTGTGCGAGGACAGTGGCTGGTACTAGTGACTACTGGGG
CCAGGGAACCCGTGTCACCGTTTCTCAGGGAGTGCATCCGCCCAACGGGCCGTGGTGGATCAGGCGCGGAGGATCTG
GCGGAGGTGGCAGCGGTGGTGGAGGCAGTAAACGACACTCAGCGAGTCTCCAGCATTTCATGTCAGCGACTCCAGGAGAC
AAAGTCAGCATCTCCTGCAAAAGCCAGCCGAGACGTTGATGATGATGGAACCTGGTACCAACAGAGACCAGGAGAACTCC
TATTTTcATTATTGAAGATGCTACTACTCTCGTTCcTGGAAATCTCACTCGATTGAGTGGCAGCGGGTATGGAACCGATT
TTACCCTCACAAATTAATACATCGATTCTGAGGATGCTGCATATTATTCTGTCTACAACATGATAATTTCCCGCTCAC
TTCGGCGGAGGACCAAGTGGAGATCAAA

Amino acid sequence of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 21]:

QVQLQWQAGALLKSWGTLSTLCAVSGASFSGYYSWIRPPPGKLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL
KLTSMTAADTAVYYCARTVAGTSDYWQGLTLVTVSSGSASAPATGGGSGGGGSGGGGSGGGGSKITLTQSPAPFMSATPGD
KVISISKASRDVDDVNWVQRPGEAIPFIIEDATTLVPGISPRFSGSGYGTDFLTITINNIDSEDAAYFCLQHDNFPLT
PGGTTKVEIK

DNA sequence of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 22]:

CAGGTACCTTGAAGGAGTCTGGTCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCTGGGTT
CTCACTCAGAACTACTGGAGAGGGTGTGGGCTGGGTCCGTGAGCCCCCAGGAAGGCCCTGGAATGGCTTGCACTCATTT
ATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACCTCCAAAAAGCAGGTG
GTCTCTTACAATGACCAACGTGGACCCAGCGGACACAGCCACTATTACTGTACACACAGGCAATACTATTATGATACAG
TGGTCAGGCATACACTTTGACTCTCTGGGCCAGGGCACCTGGTCACCGTCTCCTCAGCGCGTGGTGGATCAGCGCGCG
GAGGATCTGGCGAGGTGGCAGCGGTGGTGGAGGCGAGTAACATCCAGGTGACCCAGTCTCCATCCTCCTGTCTGCATCT
GTAGGAGACAGAGTCAACATGACTTGGCCGGCGAGTCAGGACATTAGGAAGAATTTAAATTGGTATCAGCAAAAACAGG
GAAAGCCCCTAAGGTCTGATCTACGATGCATCCGATTGGAAACAGGGATCCCATCAAGGTTCAAGTGAAGTGGATCTG
GGACAGATTTTATCCTCACCATCAGCAGCCTCGAGCTGAAGATATTGCAACATACTACTGTCAACAGTCTGATTATTTA
CCGCTCACTTTCGCGGAGGACCAAGTGGATATCAAA

Amino acid sequence of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 23]:

QVTLKESGPTLVKPTQLTLTLCTFSGFSRLRTTGEVGVWRPPPGKALEWLALIWDDDKRYSPSLKSRLLTITKDTSKKQV
VLMTNVDPADTATYYCTHEQYYIDTSGQPYFDFWQGLTLVTSSGGGSGGGGSGGGGSGGGGSGNIQVTSPLSLAS
VGDRVMTMCRAQDIRKLNWQQKPGKAPKVLIVDASDLETGIPSRFSGSGSGTDFILTISSLQPEDIATYYCQSDYL
PLTPGGGTVKDIK

FIGURE 6

DNA sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 24]:

```
CAGGTCACCTTGAAGAGTCTGGTCTACGTTGGTGAAACCCACACAGACCTCAGCGTGACCTGCACCTTGTCTGGGTT
CTCACTCAGCACTAGTGGAGTGAGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTTGAGTGGCTTGCAAGCATAA
ATTGGAATGATGATAAGTGCTACAGCCATCTCTGAAAAGCAGGCTCACCATCACCAGgACACCCCaAAAACCAGGTG
GTCCTTTGCAATGAGCAACATGGACCCCTGCGGACACAGCCACATATTCTGTGCACTCGATATGCCCCCATGATAGTGG
CCGCGAATCTTTGATGCTTCTGATGTCTGGGGCCAGGGACAATGGTCACCGTCTCTTCAGGCGGTGGTGGATCAGGCG
GCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTTCCTATGAGCTGATGCAGCTACCCCTCAGTGTCCGTGTCC
CCAGGACAGACAGCCAGCATCACTGCTCTGGAGATAATTGGGGGATAAATATGCTGTGGTATCAACAGAAGCCAGG
CCGGTCCCCCTGTGCTGTCATTATGGAGATAAACAAGCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACCTCTG
GGAACACAGCCACTCTGACCATCAGCGGACCCAGGCTATGGATGAGGCTGACTATTACTGTGAGCGTGGGACACCAGC
ACTGCTGCTCTCGGAACCTGGGACCAAGCTCACCCTCCTA
```

Amino acid sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 25]:

```
QVTLKESGPTLVKPTQTLTLTCTLSGFSLSLTSVSGVSVGWIRQPPGKALEWLASINWNDCKYSPSLKSLRITIKDTPKNQV
VLAMSNMDDPATYATSCALDMPHDSQPSQPSFASDVWVGPGTMVTVSSGGGSGGGGSGGGGSGGGSSYELMQLPSVSVS
PGQTASITCSGDLGDKYACWYQKPKRSPVLVLYGDNKRPSGIPERFSGSNSGNTATLITISGTQAMDEADYYCAQWDT
TAVFGTGTKLTVL
```

DNA sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 26]:

```
CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAGACCTGTCCCTCACTTGCACTGTCTCTGGTG
CTCCATCGGTCATGACTACTGGAGCTGGATACGSCAGCCCCCAGGGGAGGGGACTGGATGGATTGGTTTCACTCTCTTCG
ATGGGAGCAACCAACTACAACCCCTCCCTCAACGTCGAGTCACCATCTCACTCGACACCTCGAAGAATCAGCTCTCCCTG
AGGCTGACCTCTGTGACCGCTGCGGACACGCGCGTGTATTTCTGTGCGAGACTAAAGGGGGCGTGTTATTGTCTGAACC
CCCTTACTTTCAGCTCCGACGGCATGGAGCTCTGGGGCCAAAGGACACCGTCAACGCTCTCTCAGGCGGTGGTGGATCAG
GGGCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAATTTATGTGCTGACTCAGCCCCCTCAGCGCTCGGG
ACCCCGGGGAGAGGGTCAGCATCTCTTGTTCGAGGAGCAGCTCCGACATCGGAAGTAATACTGTAACCTGGTACCAACA
ACTCCCAAGGAACGGCCCCCAACTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCTGACCGATTCTCTGGCT
TCAAGTCTGCACTCAGCCTCCCTGGTCATCAGTGGCTCCAGTCTGAGGATGAGGCTGATTATTATTGTGACGATGG
GATGAGAGCTGAATGGTGTGGTGTTCGGCGGAGAACCAAGGTGACCGTCTCA
```

Amino acid sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 27]:

```
QVQLQESGPGVLKPSSETLSLCTVSGSGIGHDYNSWIRQPPGEGLEWIGFIFFDGSNTYNPSLNGRVTISLDTSKNQLSL
RLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMVWGGTQTVTVSSGGGSGGGGSGGGGSGGGGSGNFMLTQPPSASG
TPGQRVVISCSGSSSDIGSNTVNWYQQLPGTAPKLLIYNNQRPSPGVPDRFSGFSGTSASLVISGLQSEDEADYYCAAN
DESLNGVVFGGKTQVTVL
```

FIGURE 6 (cont.)

DNA sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 28]:

CAGGTGCGACTACAGCAGTGGGGCGCAGGACTGTTGAAGTCTTGGGGAACCCCTGTCCCTCACCTGCGCTGTCTCTGGTGC
GTCGTTTAGTGGTtAATTATTGGAGCTGGATCCGCCAGCCCCAGGgAAGGGGCTGGAGTGGATTGGGGAGATCAATCATC
GTGGAAGCACTACCTACAACCCGTCCTCGACGGTCGAGTCACCATATCATTAGACACATCTACCAACAGGATCTCCCTT
AAACTGACCTCTATGACCGCGCGGACACGGCCGTGTATTACTGTGCGAGGACAGTGGCTGGTACTAGTGACTACTGGGG
CCAGGGAACCCCTGGTCAACGTTTCTCAGGGAGTGATCCGCCCAACGGGCGGTGGTGGATCAGGCGGCGGAGGATCTGT
CGGGAGTGGCAGCGGTGGTGGAGGCAGTGAAACGACACTCACGCACTCTCCAGCATTTCATGTCAAGCACTCCAGGAGAC
AAAGTCAGCATCTCCTGCAAGCCAGCGGAGACGTTGATGATGATGTGAATGGTACCAACAGAGACCCAGGAGAAGCTCc
TATTTTCATTATTGAAGATGCTACTACTCTCGTTCcTGGAATCTCACCTCGATTTCAGTGGCAGCGGGTATGGAACCGATT
TTACCTCTACAATTATAACATCGATTCTCGAGGATGCTGCATATTATTCTGTCTACACATGATAATTTCCCGCTCACC
TTCGGCGGAGGGACCAAGGTGGAGATCAAA

Amino acid sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 29]:

QVQLQQWAGALLKSWGTLTSLTCAVSGASFSGYYSWIRPPGKLEWIGEINHRGSTTYNPSLDRVTISLDTSTNQISL
KLTSMTAADTAVVYCARTVAGTSDYWGQGLTVTVSSGSASAPATGGGGSGGGSGGGSGGGSETTLTQSPAFMSATPGD
KVSISCKASRDVDDVNNVYQRPGEAPIFIIEDATTLVPGISPRFSGSGYGTDFLTINNIDSEDAAYFYCLQHDNFPLT
FGGTKEIK

DNA sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 30]:

CAGGTACCTTGAAGGAGTCTGGTCTACGCTGGTGAAACCCACACAGACCCCTCAGCTGACCTGCACCTTCTCTGGGT
CTCACTCAGAACTACTGGAGAGGGTGTGGGCTGGTCCGTCAGCCCCAGGAAAGGCCCTGGAATGGCTTGCACTCATTT
ATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACCTCCAAAAGCAGGTG
GTCCTTACCAATGACCAACGTGGACCCAGCGGACACAGCCACCTATTACTGTACACACAGGCAATACTATTATGATACAG
TGCTGCGCATACTACTTTGACTTCTGGGGCAGGGCACCCCTGGTCAACCGTCTCCTCAGGGCGGTGGTGATCAGCGCGCG
GAGGATCTCGCGGAGGTGCGACCGGTGGTGGAGGCAGTAACATCCAGGTGACCCAGTCTCCATCCTCCTCTGTCTGCATCT
GTAGGAGACAGAGTCACCATGACTTCCCGGGCGAGTCAGGACATTAGGAAGAATTTAAATTTGGTATCAGCAAAAACGAG
GAAGCCCCCTAAGGTCTGATCTACGATGCATCCGATTTTGAAACAGGGATCCCATCAAGGTTTCAGTGGAAAGTGGATCTG
GGACAGATTTTATCCTCACCATCAGCAGCCTGCAGCCTGAAGATATTGCAACATACTACTGTCAACAGTCTGATTATTTA
CCGCTCACTTTTCGCGGAGGGACCAAGTGGATATCAAA

Amino acid sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 31]:

QVTLKESGPTLVKPTQLTLTCTFSGFSRLTTGEGVGWVRQPPGKALEWLALYWDKKRYSPSLKSLRLITKDTSKKQV
VLMTNVDPADTATYYCTHEQYYDTSGQPYFFDFWGQGLTVTVSSGGGSGGGGSGGGGSGGGGNIQVTSPPSSLSAS
VGDRVMTMTCRASQDIRKNLWNWQQKPGKAPKVLIVDASDLETGISPRFSGSGSGTDFILTISSLPEDIATYYCQSDYL
PLTFGGGTKEIK

FIGURE 7

Amino acid sequence alignment of variants of selected scFv antibodies against loop 6 of human CCR5

V_H region:

```

15 150 11 QVQLQESGFLVKFSETLSLTCTVGGSI--GHDYWSMIRQPPGDELEMGIFPDGSTRHSLNGRVTISLTCKNQLGLBESVTANFTVFCARLKGNHLLSPTPSSEDCMIVWGGTITTVSS CDR3
15 150 12 QVQLQESGFLVKFSETLSLTCTVGGSI--GHDYWSMIRQPPGDELEMGIFPDGSTRHSLNGRVTISLTCKNQLGLBESVTANFTVFCARLKGNHLLSPTPSSEDCMIVWGGTITTVSS
15 150 24 QVTLKESGFLVKFETQLILCTFSFSLRTIGSGVGWRQPPGQALEMALLTWDDKRTFSLSKSLTITHTSTKQVLTNTVDPADTATYCTHEQYITDSQPPY----FLPWSGGTLVTVSS

```

V_L region:

```

15 150 11 NKKLTQPPS-ASGTFQGRNISTGSSSS-DIGSNTNNWVQOLRTAPKLLTVSNRPSPGVPRPSPGKSGTSASIVISGLQSEDEADYTCAMRSEIANGVFGGKTIVTL CDR3
15 150 12 EFTLTQSPAPMSATFGKNSISCKASR--DVDDDD--VMKYQSPGCHNPFTITEDATLTLPVGISPRPSGSGXGTDFTLTINIDSEDAIYFCLQHPNF--PLTFGGGTIVKIK
15 150 24 NIQTQSPSELSASGDEWVTWTCASQ--DI--RKNLNWYQQKPKAPKVLIVDASDLGNGIPERPSGSGSGTDFLTITSLQPEDIATTYCQSD--YL-PLTFGGGTIVKIDIK

```

FIGURE 8

Amino acid sequences of variable regions of clone 15.186.35 scFv against N-terminus fragment of human CCR5

V_H region [SEQ ID NO: 34]:

QVTLKESGPTLVKPTQTLLTCTLSGFSLSSTSGVSVGWIRQPPGKALEWLASINWNDDKCYPSPSKSRLTITKDTPKNQV
VLAMSNMDPADTATYSCALDMPHPDSDGQSPDASDVWGPGTMVTVSS

V_L region [SEQ ID NO: 35]:

SYELMQLPSVSVSPGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAM
DEADYYCQAWDTSTAVFGTGKLTVL

Partial amino acid sequences of variable regions of clone 15.150.11 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 36]:

QVQLQESGPGFLVKPSETLSLTCTVSGSGIGHDYWSWIRQPPGEGLEWIGIFIPDGSTNYNPSLNGRVTISLDTSKNQLSL
RLTSTVTAADTAVYFCARLKGAWLLSEPPYFSSDGMVDVWGQTTTV

V_L region [SEQ ID NO: 37]:

NFMLTQPPSAXGTGQQRVSISSCGSSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPRDRFSGFGKSPTSASLVISGLQ
SEDEADYYCAAWDESLNGVVFSGG

Partial amino acid sequences of variable regions of clone 15.150.12 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 38]:

QVQLQQWAGALLKSWGTLSLTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL
KLTSMTAADTAVYYCARTVAGTSDYWGQGLTVTVSS

V_L region [SEQ ID NO: 39]:

TTLTQSPAFMSATPGDKVSISSKASRDVDDVNWYQQRPGEARIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDS
EDAAAYFCLQHDNFPLTFGGGKVEIK

Amino acid sequences of variable regions of clone 15.150.24 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 40]:

QVTLKESGPTLVKPTQTLLTCTFSGFSLSLTTGEGVGWVRQPPGKALEWLALIWDDDKRYPSPSKSRLTITKDTSKKQV
VLTMTNVDPADTATYYCTHEQYYDTSQGPPYDFDWGQGLTVTVSS

V_L region [SEQ ID NO: 41]:

NIQVTQSPSSLSASVGDVRTMTCRASQDIRKNLNWYQQKPGKAPKVLIIYDASDLETGIPSRFSGSGSGTDFTLTISLQP
EDIATYYCQSDYLFPLTFGGGKVDIK

FIGURE 9A

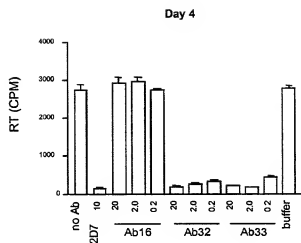


FIGURE 9B

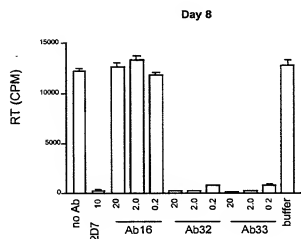


FIGURE 9C

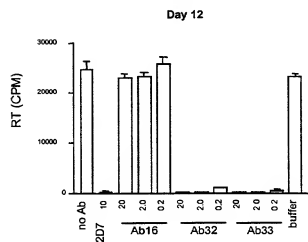


FIGURE 10A

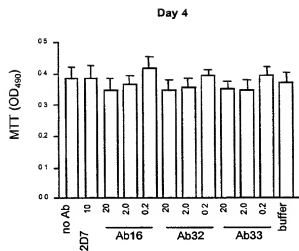


FIGURE 10B

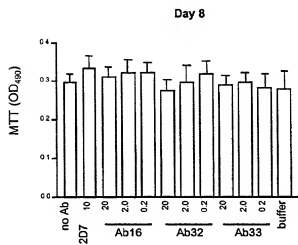


FIGURE 10C

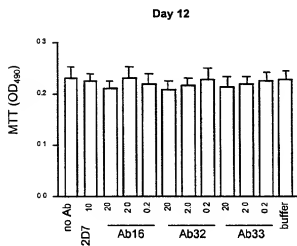


FIGURE 11A

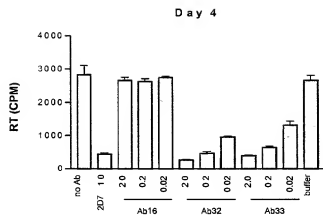


FIGURE 11B

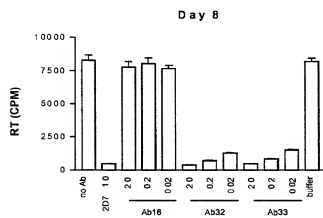


FIGURE 11C

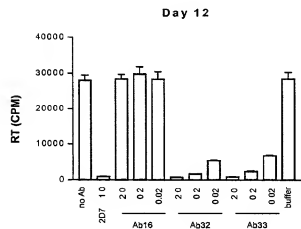


FIGURE 12

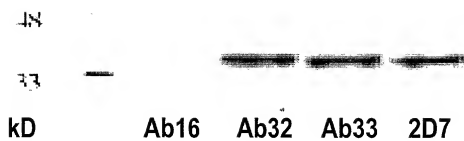


FIGURE 13

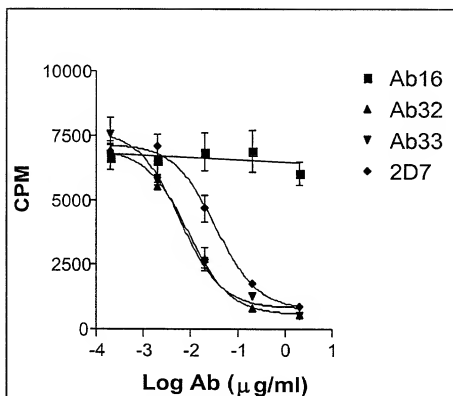


FIGURE 14

